Cell Metabolism
Obituary

John C. Lawrence, Jr. (1949–2006)

John C. Lawrence, Jr., Professor of Pharmacology at the University of Virginia, succumbed to a heart attack in Charlottesville on December 19, 2006, just days short of his 57th birthday.

John was one of the pioneers of the role of protein phosphorylation in insulin action. Never flashy, he will be remembered for his careful and rigorous approach to science. His untimely passing is a true loss for the diabetes research community.

John hailed from North Carolina, as was readily apparent from his familiar Southern accent. After attending college at Duke University, he joined the laboratory of Dr. Bill Lynn. There, John worked alongside Michael Czech, a postdoc at the time. John's time in the Lynn lab was distinguished by his companionability (which included oyster digs and long conversations about science at the beach) and his scientific accomplishments (coauthor on four papers on glucose transport in fat cells with Mike Czech and Bill Lynn). This experience changed his life.

John had initially considered following his father into medicine but decided to apply for graduate school after his experience in the laboratory. His hand-written personal statement, still on file in Charlottesville, reads in part: "During this time I have decided that research is what I want to do as it is by far the most enjoyable thing I have done. My field of interest is hormonal control of cellular metabolism. The processes of life are the most fascinating puzzle and to spend mine exploring these processes is the most rewarding way possible." John's young words were prescient.

At Charlottesville, John's thesis work with Joe Larner in the Department of Pharmacology centered on insulin signaling in primary rat adipocytes, and John made several key observations about insulin control of glycogen metabolism. After graduating in 1978, John moved on to Bill Catterall's laboratory in the Department of Pharmacology at the University of Washington for postdoctoral training with a focus on ion channels in muscle. In 1980, he joined the Department of Pharmacology at Washington University in St. Louis as an assistant professor, later rising to the rank of professor.

While in St. Louis, John played an important role in Washington University's celebrated Diabetes Center. After setting up his own laboratory, he continued with a number of significant studies of muscle but ultimately began to focus more and more on his first love, insulin signaling. In this period, John was involved in important studies on the phosphorylation of glucose transporters and MAP kinase signaling. His work showed that MAP kinase activation is not essential for acute insulin stimulation of glucose transport and glycogen synthase; he also uncovered antagonism between cyclic AMP stimulation and the MAP kinase pathway.

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However, John's research in St. Louis will likely be most remembered for his work on PHAS-1. He had long been fascinated by the idea that insulin stimulation of cells provokes not only dephosphorylation of classic metabolic targets like glycogen synthase, as discovered by his mentor Joe Larner, but also increased phosphorylation, as first described by Benjamin and by Avruch. This interest ultimately led John to identify a protein he called PHAS-1, whose serine/threonine phosphorylation was increased by insulin (Hu et al., 1994). PHAS-1 (also called 4EBP1) turned out to be a regulator of the CAP-binding protein eIF4E, which provides an important mechanistic link between insulin and the initiation of translation. John's group and that of Nahum Sonenberg published a pair of landmark papers on this subject (Lin et al., 1994; Pause et al., 1994). John went on to identify the protein kinase TOR as an upstream regulator that phosphorylates PHAS-1 (Brunn et al., 1997), and research on various aspects of the control and function of TOR continued in his laboratory until the present. John's contributions in this area were seminal.

John returned to Charlottesville in 1996 to become a professor in the department where he had been a graduate student. His scientific success continued, and he became an influential member of the Virginia diabetes research community, contributing to the University's recent success in obtaining NIH funding for a Diabetes and Endocrinology Research Center, of which he was associate director. He was valued by his colleagues

for his high scientific standards, his broad knowledge about insulin action and other biological problems, and his clear thinking. Continuing their study of proteins whose serine/threonine phosphorylation is increased by insulin, John's group identified the protein lipin as an insulin target (Huffman et al., 2002). A naturally occurring mutation of the lipin gene in fld (fatty lipid dystrophy) mice is linked to several phenotypic defects including hepatic steatosis. Lipin therefore provides a connection between insulin and lipid metabolism. Scientifically, John was at the top of his game.

A running theme of John's work over the years, noted by many of his colleagues, is its carefulness, attention to detail, and thoroughness. His data were rigorous and reliable and constituted critical foundations upon which others could rely and build. He took no shortcuts, was careful that the conclusions he drew were adequately supported, and had a talent for pinpointing weaknesses in experimental data.

Another facet of John's approach to science was his determination. While at Washington University, he applied dogged persistence and dedication to isolate and identify PHAS-1 from insulin-treated fat cells. The work was carried out in a time when protein identification and molecular cloning relied on extensive biochemical purification followed by Edman degradation. Accumulating enough PHAS-1 to sequence the protein necessitated four preparations, each starting with the fat from 50 or more rats, with 30 mCi of ^{32}P used to label each batch of adipocytes. Although John had isolated PHAS-1 in the late 1980s, he took the time and the risk to be sure he had the story just right before publishing his work.

John was also passionate as a mentor. His seriousness and dedication to his work could make him something of a tough taskmaster for those who worked for him. However, the quality of the resulting papers testified to his high standards and rigor, and most of his trainees went on to successful careers.

While John was serious about his work, he was also renowned for his keen, sometimes irreverent, sense of humor and is well remembered for his loud laugh and sense of fun. Contemporaries in the Larner laboratory recall the strains of John's enthusiastic, if somewhat less than professional, renditions of "Oh My Darling, Clementine" on the days of the monotonous adipocyte preparations.

John was as driven in his recreational activities as he was in his science. He had a great love of the outdoors and outdoor recreation. He was an avid fisherman his whole life, and while in Seattle, John became an expert in and devoted to the pursuit of the famously evasive steelhead trout. I know that while John greatly valued the scientific environment of Washington University, he missed the outdoor opportunities of the Northwest. When I first visited him upon his return to Virginia, John was especially proud of the fishing river that flowed through his rural property in Earlysville, outside of Charlottesville. For a decade, John combined his love of fishing and outdoor life in annual trips with his father to Yakutat, Alaska, in which they were dropped by a small airplane into the wilderness, lived in a forest service cabin, and fended for themselves over a week of salmon fishing. He never returned empty handed.

Backpacking was another of John's passions, and from early on, he and his wife, Linda, were enthusiastic hikers. John's annual spring break Grand Canyon hikes are legendary. For the past 15 years, he led groups that included his sons (Justin, Matt, and Robert), friends, and colleagues. Tim Haystead, a former Virginia colleague, recalls that "These were tremendous fun, but after the second day reminded one of going to boot camp." John was also a keen golfer with a single-digit handicap.

John had many other hobbies. He loved working with his hands and indeed was an accomplished carpenter, stemming from summers building beach houses back in North Carolina. Those who visited him at home saw his handiwork in the form of tables and clocks fashioned from magnificent pieces of lumber that he obtained while in the Pacific Northwest. In recent years, he obtained a few old beehives from his father, who came from a family of beekeepers. For the past two years, this had become a consuming interest for John and his son Robert, and they harvested 20 quarts of honey just last summer.

The sadness of John's untimely passing can perhaps be tempered by memories of his major scientific accomplishments, his outstanding career, and the impact he had on his family, friends, and colleagues. While we will miss John as a scientist, it seems difficult to accept that this gentle and playful personality will no longer be with us. John was as honest and honorable a person as one could ever hope to call a friend or colleague. As David James of the Garvan Institute says, "He was truly one of the good guys."

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